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| APPLICATION NUMBER | FILING DATE | FIRST NAMED APPLICANT | ATTORNEY DOCKET NO. |
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| EXAMINER | |
|---|---|
| FONDA, K | |
| **ART UNIT** | **PAPER NUMBER** |
| 1623 | 6 |

**DATE MAILED:** 06/23/99

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

## OFFICE ACTION SUMMARY

☒ Responsive to communication(s) filed on 4-14-99 and 4-30-99.

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire three month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

**Disposition of Claims**

☒ Claim(s) 1-16 is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 1-16 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

**Application Papers**

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948. Non-Subs

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. § 119**

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

**Attachment(s)**

☒ Notice of Reference Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 4 and 5

☐ Interview Summary, PTO-413

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948 Subs — Drawings NOT reviewed.

☐ Notice of Informal Patent Application, PTO-152

– SEE OFFICE ACTION ON THE FOLLOWING PAGES –

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Applicant is again advised that should claims 9-12 be found allowable, claims 13-16 will be objected to under 37 CFR 1.75 as being substantial duplicates thereof, respectively.

Applicant's arguments filed 12-23-99 have been fully considered but they are not persuasive. Applicant argues that claims 13-16 use the word "comprising". This argument is not convincing because claims 9-12 use the same word. Applicant argues that claims 9-12 require a "single formulation". This argument is not understood, because claims 9-12 have no such limitation. Provided that adequate support can be found in the specification, Applicant may wish to consider amending claims 9-12 to require a pharmaceutically acceptable carrier.

Claims 9-16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

Claims 8, 12, and 16 remain indefinite because the phrase "its derivatives" has no particular art-recognized meaning, and has not been adequately defined in the specification. Applicant's arguments filed 12-23-99 have been fully considered

but they are not persuasive. Applicant argues that the term "derivative" is fully defined on page 26 as "those having decreased toxicity, greater selectivity, [and] greater bioavailability." This argument is not persuasive. Page 26 does not define "derivative" as Applicant suggests. Rather, page 26 first states that derivatives are contemplated, and then uses the word "particularly" to introduce those derivatives "having decreased toxicity, greater selectivity, [and] greater bioavailability." Thus the particular derivatives appear to be a subset of all derivatives contemplated by Applicant. Furthermore, the particular derivatives are defined in wholly functional language, and it is not at all clear how such derivatives could be prepared or what structures they would have.

Claims 9 and 13 lack positive antecedent basis for "the resistance", "the induction", and "the increased rate" and therefore remain indefinite. Applicant's arguments filed 12-23-99 have been fully considered but they are not persuasive. Applicant argues that it is clear that none of these phrases refers back to another element. The Examiner does not agree. In fact, the use of the definite article prompts the reader to wonder whether a particular resistance, induction, or increased rate is intended. If Applicant has no such intention, Applicant should consider replacing "to reduce the resistance to the induction of apoptosis or resistance to the increased rate of

apoptosis" with --to reduce resistance to induction of apoptosis or resistance to an increased rate of apoptosis--.

Claims 9 and 13 remain indefinite because they do not state what it is that targets the recited "target cell or tissue". Applicant's arguments filed 12-23-99 have been fully considered but they are not persuasive. Applicant argues that the claim is not indefinite because it states that the resistance is mediated by a mutant EGFR. This is not persuasive because the issue is not the nature of the resistance, but rather the nature of the "target cell or tissue." Applicant may overcome this rejection by inserting --of a mutant EGFR gene-- after "tissue" in line 3 of each of claims 9 and 13.

Claims 1-16 are again rejected, as set forth in the Office action of 06-23-99 under 35 U.S.C. 103(a) as being unpatentable over HAN *et al.* (K) in view of REED (A).

Applicant's arguments filed 12-23-99 have been fully considered but they are not persuasive. Applicant argues that there is no proper motivation to combine the references, and that neither reference teaches that ΔEGFR is involved in modulation of apoptosis. This argument is not convincing. As noted in the previous Office action, HAN had taught that tyrphostin AG1478 was a relatively specific inhibitor of human glioma cells expressing ΔEGFR. Human glioma cells expressing ΔEGFR are target cells of a

mutant EGFR gene, as recited in claim 1. Furthermore, HAN had suggested that tyrphostin AG1478 could be used for treatment of glioblastomas, and breast, lung, and ovarian cancers. If tyrphostin AG1478 is a relatively specific inhibitor of human glioma cells expressing ΔEGFR, and is useful for treating cancer, then it must "modulate an apoptosis-inhibiting effect" as recited in instant claim 1. HAN need not have used these words, and need not have even understood the mechanism as Applicant does. It is sufficient that HAN's teaching, when taken in view of the teaching of REED, would have suggested to an ordinarily skilled worker to do what Applicant has done. Because REED had taught that cisplatin, taxol, and vincristine were known cancer chemotherapeutic agents which could induce apoptosis in cancer cells, and because the ability of tyrphostin AG1478 to "modulate an apoptosis-inhibiting effect" had been made clear by HAN, an ordinarily skilled worker would have expected the claimed combination therapy to be useful as claimed.

Applicant has informed the Examiner that the non-patent documents cited on the IDS form of 04-14-99 have been resubmitted as requested in the previous Office action. Unfortunately, the documents have not been matched with the file, and are not available to the Examiner at this time. The Examiner regrets any inconvenience to Applicant or to Applicant's representative. The

Examiner anticipates that the documents will be matched with the file, and will consider them when they become available.

No claim is allowed.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Papers relating to this application may be submitted to Technology Center 1600 by facsimile transmission. The number of the fax machine for official papers in Technology Center 1600 is (703) 308-4556. Any document submitted by facsimile transmission

will be considered an official communication unless the cover sheet clearly indicates that it is an informal communication.

INTERNET INFORMATION: Secure and confidential access to patent application status information is now available; see http://pto-ebc.uspto.gov for more information. Also, http://www.uspto.gov/web/offices/ac/comp/fin/clonedefault.htm may be used to pay patent maintenance fees, pay non-filing application fees, and maintain USPTO deposit accounts.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Kathleen Kahler Fonda, at telephone number (703) 308-1620. Examiner Fonda can generally be reached on Monday and Friday afternoons, and on Tuesday and Thursday mornings. If the Examiner cannot be reached, questions may be addressed to Supervisory Patent Examiner Gary Geist at (703) 308-1701. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-1235.

Kathleen Kahler Fonda, Ph.D.
Primary Examiner
Art Unit 1623